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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/882,274	06/15/2001	Alex B. Burgin JR.	P-RD 4806	7878
23601	7590	06/16/2004	EXAMINER	
CAMPBELL & FLORES LLP 4370 LA JOLLA VILLAGE DRIVE 7TH FLOOR SAN DIEGO, CA 92122			LU, FRANK WEI MIN	
			ART UNIT	PAPER NUMBER
			1634	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

8.4.

**Office Action Summary**

Application No.

09/882,274

Applicant(s)

BURGIN ET AL.

Examiner

Frank W Lu

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 03 February 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 11 is/are allowed.
- 6) ☐ Claim(s) 1,3-9,12,13,15 and 16 is/are rejected.
- 7) ☒ Claim(s) 2,10 and 14 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other:

## **DETAILED ACTION**

### ***Response to Amendment***

1. Applicant's response to the office action filed on February 3, 2004 has been entered. The claims pending in this application are claims 1-16. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of the amendment filed on February 3, 2004.

### ***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 5-7 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claim 5 recites the limitation "said polynucleotide product" in the claim. There is insufficient antecedent basis for this limitation in the claims since there is no "polynucleotide product" in step (a) and step (a) of the claim only has a ligated nucleic acid product. Please clarify.

5. Claims 6 and 16 recite the limitation "said iodonitrobenzene" in the claims. There is insufficient antecedent basis for this limitation in the claims since there is no word "iodonitrobenzene" before "said iodonitrobenzene". Please clarify.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Letsinger *et al.*, (US Patent No. 5,476,930, published on December 19, 1995).

Letsinger *et al.*, teach non-enzymatic ligation of oligonucleotides.

Regarding claim 1, since Letsinger *et al.*, teach a method of forming an oligonucleotide by: a) disposing at least two oligonucleotides in aqueous solution wherein one of the oligonucleotides has a 5' terminal bromoacetyl amino group and the other of the nucleotides has a 3' terminal phosphorothioate group; and b) covalently binding the oligonucleotides together through the  $\alpha$ -haloacyl group and the phosphothioate groups spontaneously forming a thiophosphoryl acetyl amino group therebetween (see columns 9 and 10, claims 1-7), Letsinger *et al.*, disclose contacting a polynucleotide-3' phosphorothiolate with an acceptor polynucleotide (5' terminal bromoacetyl amino group) under conditions that allow formation of a phosphodiester bond between said polynucleotide-3' phosphorothiolate and said acceptor polynucleotide, wherein a phosphodiester bond is formed between said polynucleotide-3' phosphorothiolate and said acceptor polynucleotide, whereby a ligated nucleic acid product is generated as recited in claim 1.

Therefore, Letsinger *et al.*, teach all limitations recited in claim 1.

8. Claims 1, 3, and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Albrecht *et al.*, (US Patent No. 6,013,445, published on January 11, 2000).

Albrecht *et al.*, teach massively parallel signature sequencing by ligation of encoded Adaptors.

Regarding claims 1, 3, and 4, since Albrecht *et al.*, teach that ligating (120) an encoded adaptor (having duplex polynucleotide) to an end of the polynucleotide (122) (having duplex polynucleotide), the end of the polynucleotide having a dephosphorylated 5' hydroxyl and the end of the encoded adaptor (124) to be ligated having a first strand (126) and a second strand (128), the second strand of the encoded adaptor having a 3' blocking group (130); (b) removing the 3' blocking group of the second strand after ligation by chemically removing the group in situ; (c) phosphorylating (134) the 5' hydroxyl of the polynucleotide; d) ligating (136) a second strand (142) having an unblocked 3' moiety to regenerate the encoded adaptor (138); and (e) identifying (144) one or more nucleotides at the end of the polynucleotide by the identity of the encoded adaptor ligated thereto, e.g. via a fluorescently labeled (140) tag complement (see Figure 3A and column 21, second paragraph) wherein 3' blocking group is phosphorothiolate (see column 19, second paragraph), Albrecht *et al.*, disclose contacting a polynucleotide-3' phosphorothiolate with an acceptor polynucleotide (5' hydroxyl) under conditions that allow formation of a phosphodiester bond between said polynucleotide-3' phosphorothiolate and said acceptor polynucleotide, wherein a phosphodiester bond is formed between said polynucleotide-3' phosphorothiolate and said acceptor polynucleotide, whereby a ligated nucleic acid product is generated as recited in claim 1 wherein said polynucleotide-3' phosphorothiolate further

comprises a duplex polynucleotide as recited in claim 3 and said acceptor polynucleotide further comprises a duplex polynucleotide as recited in claim 4.

Therefore, Albrecht *et al.*, teach all limitations recited in claims 1, 3, and 4.

### ***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 8, 12, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Albrecht *et al.*, (2000) as applied to claims 1, 3, and 4 above, further in view of Robbins *et al.*, (US Patent No. 5,843,648, published on December 1, 1998).

The teachings of Albrecht *et al.*, have been summarized previously, *supra*.

Albrecht *et al.*, teach all limitations recited in claims 8, 12, and 15 except a vector comprising a polynucleotide-3' phosphorothiolate as recited in claims 8, 12, and 15.

Robbins *et al.*, teach a vector with a phosphorothiolate (see column 31, lines 39-50).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claims 8, 12, and 15 using a vector comprising a polynucleotide-3' phosphorothiolate in view of the patents of Albrecht *et al.*, and Robbins *et al.*. One having ordinary skill in the art would have been motivated to do so because, comparing with a regular vector, a vector with a phosphorothiolate is not digested by exonuclease III (see column 31, lines 39-50), and the simple replacement of one kind of nucleic acid with phosphorothiolate (i.e., adaptor taught by Albrecht *et al.*,) from another kind of nucleic acid with phosphorothiolate (i.e., a vector taught by Robbins *et al.*,) during the process for performing the method recited in claims 8, 12, and 15, would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the replacement would not change the method steps of claims 8, 12, and 15.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements in such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

11. Claims 5, 9, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Albrecht *et al.*, (2000) in view of Robbins *et al.*, as applied to claims 1, 3, 4, 8, 12, and 15 above, and further in view of Panayotatos (US Patent No. 5,256,568, published on October 26, 1993).

The teachings of Albrecht *et al.*, and Robbins *et al.*, have been summarized previously, *supra*.

Albrecht *et al.*, and Robbins *et al.*, do not disclose to transform said vector comprising said acceptor polynucleotide into a host cell as recited in claims 5, 9, and 13.

Panayotatos teaches to transform a ligated vector-insert into a host cell (see column 17, last paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claims 5, 9 and 13 wherein said vector comprising said acceptor polynucleotide is transformed into a host cell in view of the patents of Albrecht *et al.*, Robbins *et al.*, and Panayotatos. One having ordinary skill in the art would have been motivated to do so because transformation of a ligated vector-insert into a host cell would generate a host cell that has an ability to increase the production of the ligated vector-insert. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to transform said vector comprising said acceptor polynucleotide into a host cell as recited in claims 5, 9, and 13.

### ***Conclusion***

12. Claim 11 is allowed over prior art in the record.



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12. Claims 2, 10, and 14 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.


14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703)872-9306 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571)272-0782.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu  
PSA  
June 10, 2004

  
**FRANK LU**  
**PATENT EXAMINER**